

Applicants : Stanley M. Crain and Ke-Fei Shen  
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Amendments to the Claims:

Please add new claims 49-99 as set forth below.

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1-29. (Canceled)

30. (Previously presented) A method for selectively enhancing the analgesic potency of a bimodally-acting opioid agonist and simultaneously attenuating tolerance associated with the administration of said bimodally-acting opioid agonist, comprising administering to a subject a composition comprising an analgesic or sub-analgesic amount of said bimodally-acting opioid agonist and an amount of an excitatory opioid receptor antagonist effective to enhance the analgesic potency of said bimodally-acting opioid agonist and attenuate tolerance associated with said bimodally-acting opioid agonist.

31. (Previously presented) The method of Claim 30, wherein the excitatory opioid receptor antagonist is selected from the group consisting of naltrexone, naloxone, etorphine, diprenorphine, dihydroetorphine, and similarly acting opioid alkaloids and opioid peptides.

32. (Previously presented) The method of Claim 30, wherein the bimodally-acting opioid agonist is selected from the group consisting of morphine, codeine, fentanyl analogs, pentazocine, buprenorphine, methadone, enkephalins, dynorphins, endorphins and similarly acting opioid alkaloids and opioid peptides.

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33. (Previously presented) The method of Claim 30, wherein the amount of the excitatory opioid receptor antagonist administered is at least 100-1000 fold less than the amount of the bimodally-acting opioid agonist administered.

34. (Previously presented) The method of Claim 31, wherein the excitatory opioid receptor antagonist is naltrexone.

35. (Previously presented) The method of Claim 34, wherein the excitatory opioid receptor antagonist is naltrexone, and is administered orally.

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36. (Previously presented) The method of Claim 32, wherein the bimodally-acting opioid agonist is morphine.

37. (Previously presented) The method of Claim 30, wherein the bimodally-acting opioid agonist is morphine and the excitatory opioid receptor antagonist is naltrexone.

38. (Previously presented) The method of Claim 32, wherein the bimodally-acting opioid agonist is methadone.

39. (Previously presented) The method of Claim 32, wherein the bimodally-acting opioid agonist is codeine.

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40. (Previously presented) The method of Claim 30, wherein the mode of administration is selected from the group consisting of oral, sublingual, intramuscular, subcutaneous and intravenous.

41. (Previously presented) A method for treating pain in a subject comprising administering to said subject a composition comprising an analgesic or sub-analgesic amount of a bimodally-acting opioid agonist and an amount of an excitatory opioid receptor antagonist effective to enhance the analgesic potency of said bimodally-acting opioid agonist and attenuate tolerance associated with said bimodally-acting opioid agonist.

42. (Previously presented) The method of Claim 41, wherein the bimodally-acting opioid agonist is selected from the group consisting of morphine, codeine, fentanyl analogs, pentazocine, methadone, buprenorphine, enkephalins, dynorphins, endorphins and similarly acting opioid alkaloids and opioid peptides.

43. (Previously presented) The method of Claim 41, wherein the excitatory opioid receptor antagonist is selected from the group consisting of naltrexone, naloxone, etorphine, diprenorphine and dihydroetorphine, and similarly acting opioid alkaloids and opioid peptides.

44. (Previously presented) The method of Claim 41, wherein amount of the excitatory opioid receptor antagonist administered is at least 100-1000 fold less than the amount of the bimodally-acting opioid agonist administered.

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45. (Previously presented) The method of Claim 43, wherein the excitatory opioid receptor antagonist is naltrexone.

46. (Previously presented) The method of Claim 42, wherein the bimodally-acting opioid receptor agonist is morphine.

47. (Previously presented) The method of Claim 41, wherein the bimodally-acting opioid agonist is morphine and the excitatory opioid receptor antagonist is naltrexone.

48. (Previously presented) The method of Claim 44, wherein the bimodally-acting opioid agonist is morphine and the excitatory opioid receptor antagonist is naltrexone.

49. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist.

50. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a delta opioid receptor agonist.

51. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a kappa opioid receptor agonist.

52. (New) The method of Claim 31, wherein the excitatory opioid receptor antagonist is naloxone.

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53. (New) The method of Claim 40, wherein the mode of administration is oral administration.

54. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist and the excitatory opioid receptor antagonist is naloxone.

55. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist and the excitatory opioid receptor antagonist is naltrexone.

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56. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a delta opioid receptor agonist and the excitatory opioid receptor antagonist is naloxone.

57. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a delta opioid receptor agonist and the excitatory opioid receptor antagonist is naltrexone.

58. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a kappa opioid receptor agonist and the excitatory opioid receptor antagonist is naloxone.

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59. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a kappa opioid receptor agonist and the excitatory opioid receptor antagonist is naltrexone.

60. (New) The method of Claim 30, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

61. (New) The method of Claim 30, wherein the amount of the excitatory opioid receptor antagonist administered is 10,000-1,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

62. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist, the excitatory opioid receptor antagonist is naltrexone, and the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered orally.

63. (New) The method of Claim 62, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

64. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist, the excitatory opioid receptor antagonist is naloxone, and the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered intramuscularly, subcutaneously or intravenously.

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65. (New) The method of Claim 64, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

66. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is morphine, the excitatory opioid receptor antagonist is naltrexone, and the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered orally.

67. (New) The method of Claim 66, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

68. (New) The method of Claim 30, wherein the bimodally-acting opioid agonist is morphine, the excitatory opioid receptor antagonist is naloxone, and the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered intramuscularly, subcutaneously or intravenously.

69. (New) The method of Claim 68, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

70. (New) The method of Claim 30 wherein the amount of the excitatory opioid receptor antagonist is 100-1000 fold less than the amount of the bimodally-acting opioid agonist administered.

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71. (New) The method of Claim 30 wherein the amount of the bimodally-acting opioid agonist administered is an analgesic amount.

72. (New) The method of Claim 30 wherein the amount of the bimodally-acting opioid agonist administered is a sub-analgesic amount.

73. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist.

74. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a delta opioid receptor agonist.

75. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a kappa opioid receptor agonist.

76. (New) The method of Claim 42, wherein the bimodally-acting opioid agonist is codeine.

77. (New) The method of Claim 42, wherein the bimodally-acting opioid agonist is methadone.

78. (New) The method of Claim 43, wherein the excitatory opioid receptor antagonist is naloxone.



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79. (New) The method of Claim 41, wherein the mode of administration is selected from the group consisting of oral, sublingual, intramuscular, subcutaneous and intravenous.

80. (New) The method of Claim 79, wherein the mode of administration is oral administration.

81. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist and the excitatory opioid receptor antagonist is naloxone.

82. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist and the excitatory opioid receptor antagonist is naltrexone.

83. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a delta opioid receptor agonist and the excitatory opioid receptor antagonist is naloxone.

84. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a delta opioid receptor agonist and the excitatory opioid receptor antagonist is naltrexone.

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85. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a kappa opioid receptor agonist and the excitatory opioid receptor antagonist is naloxone.

86. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a kappa opioid receptor agonist and the excitatory opioid receptor antagonist is naltrexone.

87. (New) The method of Claim 41, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

88. (New) The method of Claim 41, wherein the amount of the excitatory opioid receptor antagonist administered is 10,000-1,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

89. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist, the excitatory opioid receptor antagonist is naltrexone, the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered orally, and the amount of the bimodally-acting opioid agonist is an analgesic amount.

90. (New) The method of Claim 89, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

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91. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is a mu opioid receptor agonist, the excitatory opioid receptor antagonist is naloxone, the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered intramuscularly, subcutaneously or intravenously, and the amount of the bimodally-acting opioid agonist is an analgesic amount.

92. (New) The method of Claim 91, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

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93. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is morphine, the excitatory opioid receptor antagonist is naltrexone, the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered orally, and the amount of the bimodally-acting opioid agonist is an analgesic amount.

94. (New) The method of Claim 93, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

95. (New) The method of Claim 41, wherein the bimodally-acting opioid agonist is morphine, the excitatory opioid receptor antagonist is naloxone, the bimodally-acting opioid agonist and the excitatory opioid receptor antagonist are administered intramuscularly, subcutaneously or intravenously, and the amount of the bimodally-acting opioid agonist is an analgesic amount.

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96. (New) The method of Claim 95, wherein the amount of the excitatory opioid receptor antagonist administered is 1,000-10,000,000 fold less than the amount of the bimodally-acting opioid agonist administered.

97. (New) The method of Claim 41 wherein the amount of the excitatory opioid receptor antagonist is 100-1000 fold less than the amount of the bimodally-acting opioid agonist administered.

98. (New) The method of Claim 41 wherein the amount of the bimodally-acting opioid agonist administered is an analgesic amount.

99. (New) The method of Claim 41 wherein the amount of the bimodally-acting opioid agonist administered is a sub-analgesic amount.

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